

EXHIBIT 7

REISSUE LITIGATION

Docket No. 17668-A7-B/JPW/GJG

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Patentees/ Richard Axel, Michael H. Wigler, and
Reissue Saul J. Silverstein
Applicants:

Patent No.: 6,455,275 B1 Serial No.: 08/484,136

Issue Date: September 24, 2002 Filed: June 7, 1995

For : DNA CONSTRUCT FOR PRODUCING PROTEINACEOUS
MATERIALS IN EUKARYOTIC CELLS

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SIR:

**PRELIMINARY AMENDMENT TO THE
ACCOMPANYING REISSUE APPLICATION INCLUDING
STATEMENT OF STATUS UNDER 37 C.F.R. § 1.173(c)**

This Preliminary Amendment is submitted pursuant to 37 C.F.R. § 1.173(b) along with an application for reissue of the above-identified patent filed less than two years after the patent issued.

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In the Specification

Please amend the specification of the subject patent pursuant to 37 C.F.R. § 1.173(b)(1) as indicated below.

In column 1, after the first full paragraph ending on line 19, please add the following paragraph:

The invention described herein was made in the course of work under grants numbers CA-23767 and CA-76346 from the National Institutes of Health, Department of Health and Human Services. The U.S. Government has certain rights in the invention.

This amendment is made to comply with applicants' obligation under 35 U.S.C. § 202(c)(b) to include within the specification the above statement, and does not constitute new matter.

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In the Claims

Please cancel claim 4 of the Patent.

Please amend the Claims, and add new claims, pursuant to 37 C.F.R. § 1.173(b) as set forth below:

1. (Amended) A transformed Chinese Hamster Ovary cell comprising a DNA construct comprising DNA I encoding a proteinaceous material foreign to the Chinese Hamster Ovary cell and linked thereto amplifiable foreign DNA II encoding a[n amplifiable] dominant selectable phenotype, which phenotype is not expressed by such Chinese Hamster Ovary cell prior to transformation with the construct, the [construct] cell being effective for producing the proteinaceous material when the construct is introduced into the Chinese Hamster Ovary cell, wherein [the construct is] DNA I and DNA II are amplified and stably incorporated into the chromosomal DNA of the transformed Chinese Hamster Ovary cell.
6. (Amended) The transformed CHO cell of claim 5, 21, 22, or 23, wherein DNA II comprises a gene which encodes a dihydrofolate reductase [which renders the transformed CHO cell resistant to methotrexate].
7. (Amended) The transformed Chinese Hamster Ovary cell of claim 5, 21, 22, or 23, wherein the DNA I is attached to bacterial plasmid DNA.
8. (Amended) The transformed Chinese Hamster Ovary cell of claim 5, 21, 22, or 23, wherein the DNA II is attached to bacterial plasmid DNA.

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9. (Amended) The transformed Chinese Hamster Ovary cell of claim 5, 21, 22, or 23, wherein both DNA I and DNA II [is] are attached to bacterial plasmid DNA.
10. (Amended) The transformed Chinese Hamster Ovary cell of claim 5, 21, 22, or 23, wherein the DNA I is attached to phage DNA.
11. (Amended) The transformed Chinese Hamster Ovary cell of claim 5, 21, 22, or 23, wherein the DNA II is attached to phage DNA.
12. (Amended) The transformed Chinese Hamster Ovary cell of claim 5, 21, 22, or 23, wherein both DNA I and DNA II [is] are attached to phage DNA.
13. (Amended) The transformed Chinese Hamster Ovary cell of any of claims 5-12, 21, 22, or 23 further comprising the proteinaceous material.
14. (Amended) A method of producing a proteinaceous material [protein] which comprises culturing transformed CHO cells of any of claims 5-13, 21, 22, or 23 under suitable conditions to produce the proteinaceous material and recovering the proteinaceous material so produced.
15. (Amended) [The] A method of [claim 14, wherein the proteinaceous material is glycoprotein] producing a glycoprotein comprising a proteinaceous portion and a sugar portion which method comprises culturing CHO cells of any of claims 1, 3, 5-13, 16-18 or 21-23 under conditions suitable so as to produce a proteinaceous material which is a precursor of the glycoprotein and

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sugar and to synthesize or assemble the glycoprotein, and recovering the glycoprotein so synthesized or assembled, wherein amplified foreign DNA I encodes the proteinaceous material precursor of the glycoprotein.

16. (Amended) A transformed Chinese Hamster Ovary (CHO) cell which comprises amplified foreign DNA I corresponding to a gene encoding a proteinaceous material precursor of a glycoprotein of interest and amplified DNA II encoding a dominant selectable phenotype not expressed by the transformed CHO cell prior to transformation, [and] both DNA I and DNA II being stably incorporated into the chromosomal DNA of the transformed Chinese Hamster Ovary cell.
17. (Amended) The transformed Chinese Hamster Ovary cell of claim 16, wherein DNA II comprises a gene which encodes a dihydrofolate reductase [which renders the transformed cell resistant to methotrexate].
18. (Amended) The transformed Chinese Hamster Ovary cell of claim 16 or 17, wherein DNA I or DNA II is, or both DNA I and DNA II [is] are, attached to bacterial plasmid DNA or phage DNA.
21. The transformed cell of claim 5, wherein the proteinaceous material is a precursor of a glycoprotein.
22. A transformed Chinese Hamster Ovary (CHO) cell or progeny thereof which comprises amplified foreign DNA I corresponding to a gene or genes of interest which encode a proteinaceous material which is a precursor of a glycoprotein and amplified foreign DNA II encoding a

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- dominant selectable phenotype, which phenotype is not expressed by the transformed cell prior to transformation and amplification, DNA I or DNA II or both DNA I and DNA II, or neither DNA I nor DNA II being attached to bacterial plasmid DNA or phage DNA, and both DNA I and DNA II being stably incorporated into the chromosomal DNA of the transformed cell.
23. The transformed cell of claim 5, 21, or 22, wherein foreign DNA I corresponds to genes of interest.
24. The transformed Chinese Hamster Ovary cell of claim 21 or 22, further comprising a glycoprotein, which glycoprotein comprises a proteinaceous portion and a sugar portion, wherein the glycoprotein has been synthesized or assembled in the cell from proteinaceous material encoded by DNA I.
25. A process of producing a proteinaceous material which comprises culturing transformed CHO cells of any of claims 5-13, 21, 22 or 23 under suitable conditions to produce the proteinaceous material.
26. A transformed mammalian cell which comprises amplified foreign DNA I which includes a gene or genes encoding proteinaceous material which is a precursor of a glycoprotein and amplified foreign DNA II which includes a gene encoding a dominant selectable phenotype, both amplified DNA I and amplified DNA II being stably incorporated into the chromosomal DNA of the transformed cell.

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27. The transformed mammalian cell of claim 26, wherein the gene encoding the dominant selectable phenotype is a gene for a dihydrofolate reductase.
28. The transformed mammalian cell of claim 26 or 27, wherein DNA I or DNA II is, or both DNA I and DNA II are, attached to bacterial plasmid DNA or phage DNA.
29. The transformed cell of any of claim 1, 3, 5-13, 16-19, 21-24 or 26-28, wherein DNA I is not amplifiable in the cell in the absence of amplification of DNA II.
30. The transformed cell of claim 29, wherein DNA I is coamplified as a result of amplification of DNA II.
31. The transformed cell of any of claim 26-30, wherein the cell is a mouse cell.
32. The transformed cell of any of claim 26-30, wherein the cell is a human cell.
33. The transformed cell of any of claim 26-30, wherein the cell is a hamster cell.
34. A process for producing a proteinaceous material which comprises culturing transformed mammalian cells of any of claim 26-33 under suitable conditions so as to produce the proteinaceous material.
35. The process of claim 34 further comprising recovering the proteinaceous material so produced.

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36. The process of claim 34 further comprising culturing the transformed cell under suitable conditions so as to produce sugar and the precursor of the glycoprotein, and to synthesize or assemble the glycoprotein.

37. The process of claim 36 further comprising recovering the glycoprotein so synthesized.

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REMARKS

Status of Claims and Support for Amendments
Pursuant to 37 C.F.R. § 1.173(c)

Pending Claims:

- Claims 1-3 and 5-20 as issued on September 24, 2002, of which Claims 1 and 6-18 are amended herein; and
- New Claims 21-37 as added herein.

Canceled Claims:

- Claim 4 has been canceled.

Support for the amendments to the claims may be found in the '275 Patent as follows:

Support for the amendments to claim 1 may be found *inter alia*, as follows: a) amplifiable foreign DNA II at column 6, lines 34-39 and lines 45-46; b) which phenotype is not expressed at column 6, lines 37-39; c) the cell being effective at column 7, lines 45-46; and d) DNA I and DNA II are amplified and at column 6, lines 45-47.

Support for the amendment to claims 6 and 17 to recite DNA comprises a gene which encodes may be found *inter alia* at column 3, lines 46-48 and column 4, lines 57-58.

The amendments to claims 6-14 to make the claims multiply dependent is a matter of legal drafting to obtain complete protection for applicants' invention, and does not involve any question of technical support.

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The amendment to claim 14 to change "protein" to material corrects an obvious typographical error and corrects a lack of proper antecedent basis in the claim. For support, see for example, column 4, lines 22-23; and column 6, lines 19-31.

Support for the amendments to claim 15 may be found *inter alia* at column 7, lines 32-58; column 4, lines 22-23; column 3, lines 7-8 and 16-20, and column 4, lines 66-67.

Support for the amendment to claim 16 may be found *inter alia*, at column 7, lines 32-58; column 3, lines 7-8 and 16-20; and column 4, lines 22-23.

Support for the amendment to claim 18 may be found *inter alia*, at column 5, lines 42-48.

Support for new claim 21 may be found *inter alia*, at column 7, lines 32-58.

Support for new claim 22 may be found *inter alia*, at column 7, lines 32-58; column 4, lines 22-23; column 3, lines 7-8 and 16-20; column 4, lines 66-67; column 6, lines 7-18; column 7, lines 42-50; and in Figure 1.

Support for new claim 23 may be found *inter alia*, at column 7, lines 32-58; and column 6, lines 11-12; and column 7, lines 42-50.

Support for new claim 24 may be found *inter alia*, at column 7, lines 32-58.

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Support for new claim 25 may be found *inter alia*, at column 6, lines 10-18.

Support for new claims 26 and 27 may be found *inter alia*, at column 7, lines 32-58; column 3, lines 7-8 and 16-20; column 4, lines 22-23; column 6, lines 33-39, lines 44-46, and line 57 - column 7, line 17; column 2, lines 26-30; column 5, lines 60-64; and in Figure 1.

Support for new claim 28 may be found *inter alia*, at column 5, lines 42-48.

Support for new claim 29 may be found *inter alia*, at column 8, lines 26-37; column 27, lines 24-27; and column 29, lines 3-11.

Support for new claim 30 may be found *inter alia*, at column 27, lines 24-29; column 29, lines 3-11; and column 8, lines 26-37.

Support for new claims 31-33 may be found *inter alia*, at column 4, lines 64-67.

Support for new claims 34 and 36 may be found *inter alia*, at column 6, lines 10-31.

Support for new claims 36 and 37 may be found *inter alia*, at column 7, lines 32-58.

Accordingly, there is no issue of new matter associated with the amendments to any of claims 1 and 6-18 or with new claims 21-37 all of which are directed to the same general invention as originally issued claims 1-20 of the '275 Patent.

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No fee, other than the enclosed \$770.00 reissue application filing fee and the enclosed \$3,140.00 excess claims fee, is deemed necessary in connection with the filing of this Preliminary Amendment. However, if any additional fee is required, authorization is hereby given to charge the amount of any such fee to Deposit Account No. 03-3125.

Respectfully submitted,



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